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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,051	10/22/2003	Ben K. Seon	03551.0137	6113

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HODGSON RUSS LLP
ONE M & T PLAZA
SUITE 2000
BUFFALO, NY 14203-2391

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,051	SEON, BEN K.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-7 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-7 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Seon, Ben K.

Response to the Amendment

The Amendment filed on 07/20/2005 in response to the previous Non-Final Office Action (04/19/2005) is acknowledged and has been entered.

Claims 1, 5-7 and 9-13 are currently pending and under consideration.

The Declaration Under CFR 1.132 filed on 07/20/2005 by the inventor, Ben Seon, is acknowledged and has been considered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

Claims 1, 5-7 and 9-13 **remain** rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting breast tumor growth in a mammal comprising the steps of administering to a mammal SN6j and a cyclophosphamide or doxorubicin, wherein the combination of SN6j and cyclophosphoamide or doxorubicin has a synergistic effect on breast tumor growth, does not reasonably provide enablement for a method of inhibiting growth in any and/or all tumors comprising the steps of administering to a mammal any and/or all anti-endoglin antibodies in combination with a chemotherapeutic agent, wherein the combination has a synergistic effect on the inhibition of the tumor growth for the reasons of record in the prior Office Action (04/19/2005, pages 3-6) and for the reasons set forth below:

In reference to the previous office action which held that the instant specification is not enabling for claims drawn to a method of inhibiting tumor growth in a mammal comprising administering any and/or all anti-endoglin antibody or antigen binding fragment thereof and a chemotherapeutic agent, wherein the combination of the anti-endoglin antibody or antigen binding fragment and the chemotherapeutic agent has a synergistic effect on the inhibition of tumor growth, Applicants contend that claims 1, 6, 7, 9 and 10 have been amended to specify that the anti-endoglin

antibody is SN6j and that SN6j is used in combination with CPA or doxorubicin to obtain a synergistic effect on the inhibition of tumor growth and therefore, the removal of the stated rejection is respectfully requested. Applicants further assert that the Examiner argues that in order for immunotherapy to be effective, there needs to be a correlation between expression of endoglin (EDG) in normal versus tumor tissues and cites an article by the inventor indicating that EDG is not a tumor specific marker and that it is expressed in varying degrees in the vasculature of normal tissues (Int. J. Cncaer (202); 99: 310-311; page 310, 2nd column, 1st paragraph, article of record). However, Applicants respectfully points out that the same reference, in the same paragraph, states that: "Despite this limitation, we could effectively target tumor associated vasculature using select anti-EDG Mabs and immunoconjugates." In addition, Applicants argue that in the same paragraph it is also stated that "the rapidly dividing endothelial cells of tumor vasculature are much more susceptible to killing by anti-EDG Mabs than the quiescent vascular endothelium of normal tissues." Thus, Applicants submits that there is a correlation between expression of EDG in normal versus tumor tissues and that this correlation would enable one to practice the claimed method without undue experimentation.

These arguments have been carefully considered but are not found persuasive.

First, the previous rejection was based on the technical reasoning of whether the specification, as originally filed, enables a person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant claims read on a method of inhibiting tumor growth in a mammal comprising administering anti-endoglin antibody SN6j or an antigen binding fragment thereof or an anti-endoglin antibody which binds to the same epitope as SN6j or an antigen binding fragment of the anti-endoglin antibody; and a chemotherapeutic agent selected from the group consisting of cyclophosphamide and doxorubicin, wherein the combination of the anti-endoglin antibody or antigen binding fragment thereof and the chemotherapeutic agent has a synergistic effect on the inhibition of tumor growth. Thus, the claims suggest that the combination of an antigen binding fragment of SN6j or any and/or all anti-endoglin antibodies that bind to the same epitope as SN6j or any/all antigen binding fragments thereof and a chemotherapeutic agent will have a synergistic effect on inhibiting the growth of any and/or all tumors. While the Examiners acknowledges that Applicants have amended claims 1, 6, 7, 9 and 10 to specify that the anti-endoglin antibody is SN6j and that SN6j is

used in combination with CPA or doxorubicin to obtain a synergistic effect on the inhibition of tumor growth, Applicants have not provided evidence that the administration of an antigen binding fragment of SN6j or any and/or all anti-endoglin antibodies that bind to the same epitope as SN6j or any/all antigen binding fragments thereof and a chemotherapeutic agent will have a synergistic effect on inhibiting the growth of any and/or all tumors. For example, the specification, as stated in the prior office action, discloses a synergistic anti-tumor efficacy on MCF-7 breast tumors by the combination of SN6j mAb with cyclophosphamide or doxorubicin (pages 15-19, Example 6). However, a careful review of the specification does not appear to propose the mechanism by which the "unexpected" (page 2, line 32) synergism occurs, nor does the specification appear to suggest what part, e.g. domain, of anti-endoglin SN6j is responsible for the observed synergistic effect. Therefore, it would be unpredictable that a fragment of SN6j and/or any anti-endoglin antibody which binds to the same epitope as SN6j or fragment thereof could be used in a method of inhibiting tumor growth, wherein a synergistic effect is observed. The Examiner further agrees with Applicants that Seon et al. teaches rapidly dividing endothelial cells of tumor vasculature are much more susceptible to killing by anti-EDG Mabs than the quiescent vascular endothelium of normal tissues. However, Applicants have not provided evidence that the administration of SN6j and cyclophosphamide (CPA) or doxorubicin has a synergistic effect on any and/or all tumors. As noted in the prior office action, those of skill in the art recognize the unpredictability that the combination of any anti-endoglin antibodies and a chemotherapeutic agent would display a synergistic relationship on any and/or all tumors (see Wiesenthal, Maier et al , and Holmes et al.). Specifically, Weisenthal states that "true synergy is rather uncommon in most adult tumors, wherein most drug combinations in disease such as lung cancer, breast cancer, and ovarian cancer are merely additive (whole equals the sum of its parts) and not synergistic." Thus, it would not be predictable that the synergistic effect observed in the growth of the breast tumor lines would be indicative to any tumor and as such, the method would require undue experimentation by one of skill in the art to practice the invention as claimed.

Therefore, NO claim is allowed

All other rejections and/or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Brandon J Fetterolf, PhD
Examiner
Art Unit 1642

BF

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER
9/16/05